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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/806,689	07/13/2001	Boris Tartakovsky	TARTAKOVSKY 1	5905

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EXAMINER	
EWOLDT, GERALD R	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 04/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/806,689	TARTAKOVSKY ET AL.	
	Examiner	Art Unit	
	G. R. Ewoldt, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 August 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) *1-7,18-20 and 22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-17 and 21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election of Group IV, Claims 13-17 and 21, filed 8/07/03, with traverse, is acknowledged.

Applicant traverses the restriction of Groups III (Claims 8-12 and 21) and IV to separate groups in that both inventions are linked to the detection of MO2.

Groups III and IV are hereby rejoined.

2. Claims 1-7, 18-20 and 22 are withdrawn from further consideration by the Examiner, under 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

Claims 8-17 and 21 are pending and under examination.

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 8-17 and 21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, specifically:

A) In Claims 8 and 13, the actual method steps would properly be recited in the same tense. For example, given that the first step of the claims comprises "obtaining", the second step of the claims would properly be "separating", the third step would be "fixating and permeablizing", etc.

B) In Claim 8, steps v-vii are missing, accordingly, step x, which refers to step v, is nonsensical.

C) In Claim 8 it is unclear precisely what is determined in step x and what said determination would indicate. It is clear that a comparison is made between the number of MO2+ cells in a subject individual and a set of healthy controls, but it is unclear precisely what the comparison means. As recited, it appears that the claim indicates that if even one more cell is positive in the subject individual, said individual would have a high probability of having an infection. This same problem occurs in Claims 9, 13, and 14.

D) In Claims 9 and 14, "T cells specific antigens" would properly be "T cell-specific antigens".

E) In Claim 21, it is unclear precisely what an "MO2-RD1mab" is. Whereas the term could be intended to encompass any antibody

labeled with Red Dye No.1 that binds MO2, it might also be intended to encompass only a specific antibody from a specific source, e.g., a laboratory designation intended to encompass a specific antibody from the Inventors' laboratory. Accordingly, the term renders the claim vague and indefinite.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 8-17 and 21 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Specifically, the specification provides insufficient evidence that the claimed method could be used to identify individuals with a high probability of having an infection or monitor the efficacy of a treatment.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as claimed without an undue amount of experimentation. Undue experimentation must be considered in light of factors including: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill in the art, the level of predictability of the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention.

Regarding novel methods involving biological processes, "The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature

of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling (MPEP 2164.03)". The MPEP further states that physiological activity can be considered inherently unpredictable. The state of the medical arts are such that relatively little is known regarding the claimed method of assaying CD14 levels employing an antibody to the MO2 epitope as a measure of infection or the efficacy of treatment for infection.

It is noted that given the language of the instant claims the claimed invention is intended to encompass significant breadth, i.e., methods of monitoring *any and all* types of infection, including but not limited to, bacterial, viral, fungal, and parasitic infections. For the invention to function then, it would be required that it be established that increased CD14 be present in the T cells of individuals suffering from *any and all* types of infections. Additionally, for the claimed method of monitoring the efficacy of a treatment to be enabled, it would be necessary that the specification establish that CD14 levels are reduced in response to efficacious treatment. Accordingly, it appears then that, given their novelty and considering their breadth, the enablement of the claimed methods would require a significant disclosure representative of all of the infections and all of the treatments encompassed by the claims. Said disclosure would most obviously take the form of the measurement of CD14 in T cells in a representative number of infectious models or infection types, accompanied by the measure of the reduction of CD14 in T cells after a representative number of treatments of said infections. Additionally, other limitations (as discussed below) would also require enablement.

A review of the specification discloses just three relevant examples (4, 5, and 6), the data from which are set forth in Tables 1 and 2 and Figures 10, 11, and 12. Example 4 (Figures 10, 11, and 12) asserts that some individuals suffering from bacterial sepsis and HIV infection display increased MO2 in CD3+ cells. However, the figure legends disclose only "various kinds of infections" while Figures 10 and 12 themselves discloses only "infectious diseases" and Figure 11 itself discloses only "individuals". It is thus impossible to evaluate whether or not the diseases and subjects of the example are representative of those encompassed by the claims. In fact, the example and figures are essentially impossible to interpret given the lack of specific information disclosed in them. Example 5 (Table 1) discloses that MO2 is seen at higher levels in γ/δ T cells. It

is unclear how this information could relate to the infected or treated individuals of the claims. Example 6 (Table 2) discloses that asymptomatic HIV+ patients show more MO2 in their T cells. Table 3 shows that 2 of 4 treated HIV+ patients showed a decrease in MO2 while 2 of 4 treated patients did not. In total then, it appears that the examples demonstrate only that: 1) MO2 may be increased in the T cells of HIV+ patients, and 2) that decrease in MO2 levels cannot be used as an accurate or reliable measure of the efficacy of treatment in HIV+ patients. This limited disclosure cannot be considered to be representative (nor enabling) of the scope of the claims.

Regarding additional limitations not enabled by the specification, there is no showing that the MO2 antigen is ever "expressed" by T cells. Indeed, the Inventors' own work (Tartakovsky et al., *Immunol. Letts.*, 2003) teaches that the protein is most likely not expressed at all by T cells, but rather it is internalized from an external source. Regarding the limitations of Claims 10-12 and 15-17 regarding the types of T cells employed in the comparisons to healthy cell populations, the specification discloses only that HIV+ CD8+ T cells show increased MO2 levels. In the case of CD4+ T cells, again only HIV+ cells are employed and in this instance the standard deviations approach (or exceed) the percentage of positive cells. Regarding γ/δ T cells, there is no disclosure comparing healthy to infected cells with any infectious agent.

It is the Examiner's position then that this limited disclosure is insufficient support for the methods of the instant claims. *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. Thus, in view of the quantity of experimentation necessary, the lack of sufficient working examples, the unpredictability of physiological activity, the lack of sufficient specific guidance in the specification, and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

7. No claim is allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (571) 272-0843. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail

service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

Please Note: Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

4/6/04

G.R. EWOLDT, PH.D.
PRIMARY EXAMINER

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